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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,689	11/24/2003	Mario Stevenson	UMY-034	3913

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/722,689	STEVENSON ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44 and 75-94* is/are pending in the application.

4a) Of the above claim(s) *23-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 75-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/2704; 11/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner and Art Unit in charge of this Application have changed. Please address further correspondence to Richard Schnizer, Art Unit 1635, whose contact information is given at the end of this Action.

An amendment was received and entered on 11/17/06. Applicant's election without traverse of group 1 is acknowledged.

Claims 45-74 were cancelled and new claims 75-94 were added as requested.

Claims 23-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/17/06.

Claims 1-44 and 75-93 are pending.

Claims 1-22 and 75-94 are under consideration in this Office Action.

Specification/Compliance with Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s). Applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). **The specification at page 31, line 9, discloses the sequence**

TCTCTGGTTAGACCAGATCTG, and identifies it as SEQ ID NO:12. However, this sequence is not disclosed in the instant Sequence Listing, and SEQ ID NO:12 appears to be a different sequence (see e.g. page 31, line 8, and the Sequence Listing). Applicant must provide:

A substitute computer readable form (CRF) copy of the "Sequence Listing" containing the sequence in question.

A substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

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For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.
- Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 22 is drawn to the genus of proteins that can associate with an siRNA complementary to an HIV genome, wherein the proteins recognize the portion of the HIV genome to which the siRNA is complementary. The specification as filed fails to disclose a single example of any such protein. The only portion of the specification as filed that appears to support this genus is at page 6, lines 9-11, which states: "[t]he term "siRNA complex" refers to a complex of siRNA and proteins that recognize and degrade RNAs with a sequence sufficiently homologous to that of the siRNA." These passage appears to refer to DICER or similar endonucleases that use siRNA as a guide sequence in the process of cleaving target RNAs. The nature of such proteins is that they do not recognize any specific sequences, instead they rely on the siRNA guide strand to provide sequence recognition. As a result, one of skill in the art could not conclude that Applicant was in possession of the claimed genus at the time of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-22 and 75-93 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Lois-Caballe et al (US 20030059944 A1).

Lois-Caballe taught methods and compositions for producing siRNAs from retroviral vectors, including shRNAs directed against any region of about 19-25 nucleotides in length of the 9-kb transcript of the integrated HIV virus HIV genes. See paragraph 142 which states that in one embodiment of the invention, a retroviral construct has an RNA coding region that encodes a double stranded molecule having at least 90% homology to the HIV viral RNA genome, an expressed region of the HIV viral genome, for example, to any region of about 19-25 nucleotides in length of the 9-kb transcript of the integrated HIV virus, or any of the variously spliced mRNA transcripts of HIV. Target regions within the HIV transcripts can be chosen to correspond to any of the viral genes, including, for example, HIV-1 LTR, vif, nef; and rev. Thus Lois Caballe anticipates siRNAs of 19-25 nucleotides directed against any known HIV coding region

including gag, pol, and env genes. See paragraphs 152 and 159 for disclosure of shRNAs.

Claim 10 is included in this rejection because it is a product by process claim where, absent evidence to the contrary, the product of Lois-Caballe is identical to the claimed product. Similarly, claims 13 and 86 are included in this rejection because, although Lois-Caballe did not teach expression from a plasmid vector, there is no difference between an siRNA produced from a plasmid vector and one produced from a lentiviral vector. The claims are drawn to an siRNA, not to a method of making the siRNA. Absent evidence to the contrary, there is no difference between the siRNAs made by plasmid vectors, retroviral vectors, or synthetic chemistry.

Claims 20 and 21 are included because Lois-Caballe contemplates siRNA that are only 90% identical to the target, which would necessarily have mismatched bases. The mismatched bases are considered to be modified bases since they differ from the base that would be complementary to the target.

Claim 22 is included in this rejection because interaction of the siRNAs of Lois-Caballe with DICER is inherent in their process of use. Although one of skill in the art would not necessarily conclude that DICER recognizes any portion of HIV, the only portion of the instant specification supporting claim 22 appears to refer to the siRNA/DICER complex. See page 6 lines 9-11 which state: "[t]he term "siRNA complex" refers to a complex of siRNA and proteins that recognize and degrade RNAs with a sequence sufficiently homologous to that of the siRNA."

Claims 75 and 80 are included because Lois-Caballe fairly teaches siRNAs against any HIV coding region, including pol. Similarly claim 78 is included because one of skill in the are would recognize these coding regions as including env.

Claims 88-93 are included in this rejection because although they recite structural requirements of a vector (e.g. the vector must encode a plurality of siRNAs), these vector structure requirements are given no patentable weight because the claims are drawn to "a small interfering RNA (siRNA)", and not to a vector. The particulars of the vector are not considered to have any effect on the structure of the claimed siRNA, and so are given no patentable weight.

Claims 1-3, 7-19, 22, 75, 76, 79, 80, and 83-94 are rejected under 35 U.S.C. 102(e) as being anticipated by Engelke et al (US 20030148519 A1).

Engelke taught methods and compositions for vector-driven intracellular expression and delivery of siRNAs of about 18-25 base pairs. See abstract and paragraphs 10, 105, and 109. Inhibition of HIV pol is exemplified at paragraphs 282-284. See also paragraphs 158 and 245.

Claim 10 is included in this rejection because it is a product by process claim where, absent evidence to the contrary, the product of Engelke is identical to the claimed product. Similarly, claims 13 and 86 are included in this rejection because, although Engelke did not teach expression from a plasmid vector, there is no difference between an siRNA produced from a plasmid vector and one produced from a lentiviral vector. The claims are drawn to an siRNA, not to a method of making the siRNA.

Absent evidence to the contrary, there is no difference between the siRNAs made by plasmid vectors, retroviral vectors, or synthetic chemistry.

Claims 88-93 are included in this rejection because although they recite structural requirements of a vector (e.g. the vector must encode a plurality of siRNAs), these vector structure requirements are given no patentable weight because the claims are drawn to "a small interfering RNA (siRNA)", and not to a vector. The particulars of the vector are not considered to have any effect on the structure of the claimed siRNA, and so are given no patentable weight.

Claims 1-11, 14-22, 75-84, and 86-94 are rejected under 35 U.S.C. 102(e) as being anticipated by McSwiggen (US 20030175950 A1).

McSwiggen taught RNA interference mediated inhibition of HIV gene expression using short interfering RNA. The siRNA of the invention can be unmodified or chemically modified. The siRNA of the instant invention can be chemically synthesized, expressed from a vector or enzymatically synthesized. The instant invention also features various chemically modified synthetic short interfering RNA (siRNA) molecules capable of modulating HIV gene expression/activity in cells by RNA inference (RNAi). See paragraph 11. McSwiggen contemplates inhibition of any HIV coding sequence, including for example LTR, nef, vif, tat, or rev. See paragraphs 12, 23, and 110.

In another embodiment, the invention features one or more siRNA molecules and methods that independently or in combination modulate the expression of gene(s) encoding the HIV-1 envelope glycoprotein. See paragraph 13.

In one embodiment, nucleic acid molecules of the invention that act as mediators of the RNA interference gene silencing response are double stranded RNA molecules. In another embodiment, the siRNA molecules of the invention consist of duplexes containing about 19 base pairs between oligonucleotides comprising about 19 to about 25 nucleotides, for example, about 19, 20, 21, 22, 23, 24 or 25 nucleotides. In yet another embodiment, siRNA molecules of the invention comprise duplexes with overhanging ends of 1-3 (i.e., 1, 2 or 3) nucleotides, for example 21 nucleotide duplexes with 19 base pairs and 2 nucleotide 3'-overhangs. These nucleotide overhangs in the antisense strand are optionally complimentary to the target sequence. See paragraph 28.

In another embodiment, the invention features a method for modulating the expression of more than one HIV gene within a cell, comprising: (a) synthesizing siRNA molecules of the invention, which can be chemically modified, wherein one of the siRNA strands includes a sequence complimentary to RNA of the HIV genes; and (b) introducing the siRNA molecules into a cell under conditions suitable to modulate the expression of the HIV genes in the cell. See paragraph 67

Claims 88-93 are included in this rejection because although they recite structural requirements of a vector (e.g. the vector must encode a plurality of siRNAs), these vector structure requirements are given no patentable weight because the claims are drawn to "a small interfering RNA (siRNA)", and not to a vector. The particulars of the vector are not considered to have any effect on the structure of the claimed siRNA, and so are given no patentable weight.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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